REMARKS

Claims 1-6, 9-12, 15-18, and 20-26 are in this application. Claims 1-6, 9-12, 18 and 21-26 are withdrawn. Claims 7, 8, 13, 14 and 19 have been cancelled. Claims 15, 16, 17, and 20 have been amended. The amendments to these claims will be discussed below.

Multiple Dependent Claim 16

Claim 16 has been amended to depend from claim 15. Claims 13 and 14 have been cancelled. Claim 16 has also been amended to include the subject matter of withdrawn claims 1, 2 and 3. Therefore, it is respectfully requested that the objection to claim 16 be withdrawn.

Sequence Listing

A substitute sequence listing accompanies this response.

Specification

Pages 3 and 4 have been amended to delete the hyperlinks. The other amendments were made to correct obvious clerical errors.

Claim Objections

Claim 19 has been amended to correct the spelling of familial.

35 USC 101

Claims 15, 17, 19 and 20 have been rejected under 35 USC 101 because according to the Examiner the claimed invention is directed to non-statutory subject matter. The Examiner characterizes these claims as methods for diagnosis comprising the single step of detecting in a biological sample of an individual the 313+insT mutation. The Examiner states that there is no required transformation of an article or physical object to a different state and thus, according to In re Bilski these claims do not define statutory subject matter. This is respectfully traversed.

Carrying out the methods of these claims require a physical transformation. Claim 15 defines an extracorporeal method of in vitro diagnosis of familial hypercholesterolemia comprising detection in a biological sample. Extracorporeal means situated or occurring outside the body and a standard definition of in vitro is in an artificial environment outside a living organism. Clearly the biological sample used in an extracorporeal method of in vitro diagnosis is a physical object that must be in a different state than it was in the body. Therefore, claims 15, 17, 19 and 20 comply with 35 USC 101.

However, to expedite prosecution, claim 15 has been amended to define detecting in a biological sample that comprises nucleic acids of subject from which the sample was obtained.

Therefore it is respectfully requested that this rejection be withdrawn.

35 USC 112, second paragraph

The Examiner has rejected claims 15, 17, 19 and 20 as being unclear by reciting the term 313+1insT. This is respectfully traversed.

As described in the specification, the mutations listed in Table I on page 9 of the specification are identified according to the scientifically approved nomenclature. Therefore, one of skill in the art would be able to identify this mutation based on their knowledge and the specification.

Claim 19 has been amended to include wherein the 313+1insT mutation is detected by detecting the presence of at least one of SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58 and SEQ ID NO:59 in the junction of exon 3 and intron 3 in the low density lipoprotein receptor (LDL-r) gene wherein the presence is 313+1insT is indicative of a diagnosis of familial hypercholesterolemia,. Support for this amendment is found in the specification on page 24, lines 6-7 and example 3

Therefore, it is respectfully requested that this rejection be withdrawn.

35 USC 112, first paragraph,Written Description

According to the Examiner, claims 15, 17, 19 and 20 do not comply with the written description requirement. This is respectfully traversed.

For the reasons explained above in reference to the rejection under 35 USC 112, second paragraph, the claims comply with the written description requirement.

Therefore, it is respectfully requested that the rejection be withdrawn.

35 USC 112, first paragraph, Enablement

Claims 15, 17, 19 and 20 are rejected under 35 USC 112, first paragraph as not being enabled. This is respectfully traversed.

Being filed with the Information Disclosure Statement that accompanies this response are the following references that describe the relationship between the claimed mutations and familial hypercholesterolemia.

1) Tejedor, Diego, et al. "Reliable Low-Denisity DNA Array Basd on Allele-Specific Probes for Detection of 118 Mutations Causing Familial Hperchlosterolemia", Clinical Chemistry Vo. 51:7 pages 1137-1144 (2005); (See discussion beginning on page 1141 that describes the use of DNA array a specific tool for genotyping the FH-

causing mutations in the Spanish population. There are detection rates of from 60-80% in populations that have very strict clinical inclusion criteria, such as coronary heart disease, decreased LDLR activity, the presence of xanthomas, or a Dutch MEDPED score.)

2) Alonso, R. "Cardiovascular disease in familial hypercholesterolaemia: Influence of low-density lipoprotein receptor mutation type and classic risk factors" , Atherosclerosis, pages 1-7 (2008); (page 2, first column- Familial hypercholestoremia is caused by mutations in the gene encoding the low-density lipoprotein receptor (LDLR).
3) Civerira, Fernando, et al. "Comparison of Genetic Versus Clinical Diagnosis in Familial Hypercholesterolemia" The American Journal of Cardiology(www.AJConline.org) , pages 1-7 (2008); (Page 1, column 2, genetic testing is the preferred diagnostic method for FH because it provides an unequivocal diagnosis.)
4) Junyent, Mireia, et al. "Femoral Atherosclerosis in Heterozygous Familial Hypercholesterolemia: Influence of the Genetic Defect", Arterioscler Thromb Vasc Biol Vol. 28, pages 580-586 (2008) (Page 580, column 1, "Despite the use of stringent clinical criteria, only the detection of molecular defects provides an unequivocal diagnosis of FH." and
5) Mozas Pilar, et al. "Molecular Characterization of Familial Hypercholesterolemia in Spain: Identification of 39 Novel and 77 Recurrent Mutations in LDLR", Human Mutation Mutation in Brief Vol. 735 Pages 1-13 (2004) (see page 5 line 3 and Table 2 on page 7 that shows that this mutation was identified in patients with familial hypercholesterolemia).

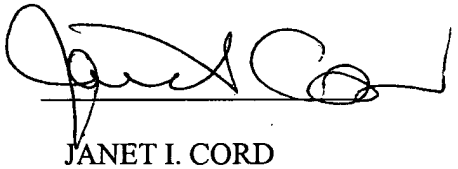
These references demonstrate that the mutations can be used to identify familial hyperchosteromia.

In addition, as described in the text under Table 1 on page 7 of the Mozas article, the nomenclature used for the mutations is that recommended by Antonarakis et al. (1998) and den Dunnen et all (2000). Therefore, one of skill in the art would be able to identify the 313+1insT mutation as recited in the claims.

Accordingly, one of skill in the art would be able to make and use the invention and as such it is enabled. It is respectfully requested that the rejection be withdrawn.

Accordingly, it is submitted that the present application is in condition for allowance and favorable consideration is respectfully requested.

Respectfully submitted,



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